

**Table 1. *In vivo* transduction efficiency of nNOS in liver cells from normal and injured livers**

Cell Type	Normal	BDL	CCl <sub>4</sub>
H	41.9 ± 3.3	39.2 ± 3.3	37.3 ± 3.1
SEC	63.1 ± 7.8	52.7 ± 4.8 *	41.2 ± 3.6*
HSC	65.9 ± 4.5	50.4 ± 2.9*	40.4 ± 2.7*

Ad.nNOS was administered via the femoral vein ( $1.5 \times 10^{11}$  pfu/kg). For BDL rats, ad.nNOS was infused 2 days after BDL, and for CCl<sub>4</sub> injury, virus was given 2 days after the 10th dose. Cell harvest was performed 7 days after adenovirus administration. After cell isolation, cells were allowed to adhere for 18 hours and NADPH-diaphorase staining was performed. Numbers shown represent percent of total NADPH-diaphorase positive cells (i.e. transduced with nNOS, n=3). \*P < 0.05 vs. normal. Abbreviations: H, hepatocyte; SEC, sinusoidal endothelial cells; HSC, hepatic stellate cell; BDL, bile duct ligation; CCl<sub>4</sub>, carbon tetrachloride

**Table 2. Relative NO (nitrite) production in normal and injured liver cells after *in vivo* gene transfer**

Cell Type	Normal			BDL			CCl <sub>4</sub>		
	Control	Ad. $\beta$ -gal		Control	Ad. $\beta$ -gal		Control	Ad. $\beta$ -gal	
		Ad.nNOS	Ad.nNOS		Ad.nNOS	Ad.nNOS		Ad.nNOS	Ad.nNOS
H	0.2±0.0	0.2±0.0	1.3±0.3*	0.3±0.0	0.4±0.0	1.3±0.3*	0.2±0.0	0.2±0.0	0.3±0.1*
SEC	5.7±0.1	5.6±0.1	8.9±0.4*	10.8±0.2	11.4±0.3	16.9±0.5*	0.4±0.0	0.4±0.0	2.1±0.4*
HiSC	0.4±0.1	0.4±0.1	6.2±0.8*	2.0±0.5	1.9±0.3	4.4±0.8*	0.3±0.1	0.3±0.1	1.3±0.3*

Methods: Liver injury was induced as in Table 1. Ad. $\beta$ -gal or Ad.nNOS were administered via femoral vein  $1.5 \times 10^1$  pfu/kg two days after BDL, or the last dose of CCl<sub>4</sub>. Liver cells were isolated 7 days later and were cultured for 24 hours after which nitrite concentrations in conditioned supernatants were determined. Shown are means ± SEM ( $\mu$ M/ $\mu$ g protein). \*p<0.05 for Ad.nNOS transfected compared with control or Ad. $\beta$ -gal transfected (n=3, for each condition). Abbreviations: H, hepatocyte; SEC, sinusoidal endothelial cells; HiSC, hepatic stellate cell; BDL, bile duct ligation; CCl<sub>4</sub>, carbon tetrachloride

**Table 3. Effect of transduced nNOS on portal pressure**

		Perfusion Pressure (cmH <sub>2</sub> O)				
Transduction State		Flow Rate (ml/min)			P <sub>Q=0</sub> (cmH <sub>2</sub> O)	Slope <sub>PQR</sub> (cmH <sub>2</sub> O.min. ml <sup>-1</sup> )
		20	30	40	50	
Normal		4.1 ± 0.2	5.6 ± 0.4	7.4 ± 0.7	10.4 ± 0.5	0.81 ± 0.10
CCl <sub>4</sub>						
Ad.β-gal		8.5 ± 0.5 <sup>#</sup>	11.1 ± 0.9 <sup>#</sup>	14.7 ± 0.1 <sup>#</sup>	16.9 ± 0.3 <sup>#</sup>	0.28 ± 0.02 <sup>#</sup>
Ad.nNOS		6.3 ± 0.2 <sup>#,*</sup>	8.7 ± 0.3 <sup>#,*</sup>	12.0 ± 0.2 <sup>#,*</sup>	14.9 ± 0.4 <sup>#,*</sup>	1.16 ± 0.03 <sup>#,*</sup>
BDL						
Ad.β-gal		8.8 ± 0.1 <sup>#</sup>	11.0 ± 0.6 <sup>#</sup>	13.6 ± 0.5 <sup>#</sup>	15.4 ± 0.6 <sup>#</sup>	3.32 ± 0.17 <sup>#</sup>
Ad.nNOS		7.4 ± 0.1 <sup>#,*</sup>	9.0 ± 0.2 <sup>#,*</sup>	11.2 ± 0.4 <sup>#,*</sup>	13.9 ± 0.4 <sup>#,*</sup>	2.00 ± 0.10 <sup>#,*</sup>
7-NI		9.1 ± 0.1 <sup>#</sup>	11.9 ± 0.2 <sup>#</sup>	13.8 ± 0.1 <sup>#</sup>	16.2 ± 0.2 <sup>#</sup>	3.33 ± 0.22 <sup>#</sup>
7-NI/Ad.nNOS		9.0 ± 0.3 <sup>#¶</sup>	11.6 ± 0.2 <sup>#¶</sup>	13.5 ± 0.3 <sup>#¶</sup>	15.8 ± 0.5 <sup>#¶</sup>	3.24 ± 0.10 <sup>#¶</sup>
						0.26 ± 0.05 <sup>#</sup>

Liver injury (BDL or CCl<sub>4</sub>) was as in Example 1. Either Ad.nNOS or Ad.β-gal (each 1.5×10<sup>11</sup> pfu/kg) were injected via the femoral vein 7 days prior to isolated liver perfusion. Portal pressure, monitored continuously, was recorded at incremental flow rates and portal resistance was calculated. In experiments where 7 NI was used, this compound was administered by intraperitoneal injection one day prior to BDL (25 mg/kg) and every 2 days thereafter. <sup>#</sup>P<0.05 vs. normal; <sup>\*P<0.05 vs. Ad.β-gal for each injury model; <sup>¶</sup>P<0.05 vs. Ad.nNOS (all, n=4). Abbreviations: BDL = bile duct ligation; CCl<sub>4</sub> = carbon tetrachloride; P<sub>Q=0</sub> = flow inlet pressure; Slope<sub>PQR</sub> = regression slope of multiple point pressure flow relationships; 7-NI = 7-nitroindazole.</sup>